REMARKS

Claims 1-79 were pending in the application. Claims 1-29 and 36-37 were withdrawn from consideration as directed to non-elected inventions.

The specification has been amended to increase the line spacing in the tables.

Claims 30, 32, 33, and 35 have been amended. Support for the amendments can be found throughout the specification as originally filed.

New claims 80-87 have been added. Support for new claims 80-87 can be found throughout the specification and claims as originally filed.

Claim 34 has been canceled.

Upon entry of this amendment, claims 30-33, 35, and 80-87 will be pending.

No new matter has been added.

Objections

Claims 30 to 35 stand objected to as being dependent upon non-elected claims. Claims 30 to 35 have been amended removing the dependency on non-elected claims, rendering the objection moot.

Claims 30 to 35 stand objected to under 37 C.F.R. § 1.75(c), as allegedly being of improper dependent form. Claims 30 to 35 have been amended, rendering this objection moot.

The Office objected to the tables presented on pages 11, 26, 27, 59, and 60 of the specification as filed because the tables allegedly do not comply with 37 C.F.R. § 1.52(b) with respect to line spacing. Applicants respectfully disagree. However, in order to advance prosecution, Applicants have amended the specification so that the tables have line spacing of at least 1.5 lines.

In view of the foregoing, Applicants respectfully request that the objections to the specification and the claims be withdrawn.

Rejection under 35 U.S.C. § 101

Claims 30-35 stand rejected under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by a specific, substantial and credible asserted utility or a well established utility. Applicants respectfully disagree.

Utility Examination Guidelines

The Utility Examination Guidelines require that a claimed invention have a specific, substantial and credible asserted utility, or, alternatively a well-established utility. As Applicants have asserted utilities that are specific, substantial and credible and well-established, the Utility Requirement has been satisfied. Applicants therefore respectfully request the withdrawal of the rejection under 35 U.S.C. § 101.

The Utility Examination Guidelines require a claimed invention to have a utility that is specific to the subject matter claimed (a "specific utility"). The present application recites at, for example, pages 37-42 of the specification that the claimed invention can be used, *inter alia*, to identify ligands and/or protein binding partners. Additionally, the polypeptides of the present invention can be used to generate antibodies useful to localize the protein *in vivo* or *in vitro*. For example, the specification teaches that nGCPR-2664 (SEQ ID NO: 2) is strongly expressed in brain, heart, kidney, peripheral blood leukocytes and lung and is also expressed in the testis. Thus, antibodies generated against nGPCR-2664 can be used to identify the origin of cells and/or tissues as being from the brain and/or specific areas of the brain. Being able to identify specific cell types is also useful for identifying defects and abnormalities in the tissues by the absence or presence of staining of nGPCR-2664. Thus, there is no question that Applicants have asserted at least one specific utility and, in fact, have provided numerous specific utilities for the polypeptides of the present invention.

Additionally, the Office appears to be under the assumption that ***absolute*** certainty is required for a polynucleotide to have a specific utility. The standard applicable in this case is not, however, proof to certainty, but rather proof to reasonable probability. As the Supreme Court stated, applicant need only prove a "substantial

likelihood" of utility; certainty is not required. *Brenner v. Manson*, 383 U.S. at 532. Although there may be numerous inventions that may arise from the present application, this standard does not justify the Office's stance that the present invention lacks a specific utility. Thus, Applicants have complied with the specific utility requirement.

The Claimed Invention Has A Substantial Utility

The Utility Examination Guidelines also require that a claimed invention have a utility that defines a real-world use (a "substantial utility"). Applicants teach, as described above, that the claimed invention can be used to make antibodies, identify ligands and other binding partners, such as other proteins that interact with the polypeptide (i.e., a G protein). Thus, it is clear that the claimed invention has real-world uses. All the uses described in the present application are real-world uses and stand in stark contrast to the "throw away" uses (e.g., landfill component or snake food) set forth in the utility guidelines. Thus, there is no question that Applicants have asserted at least one substantial utility and, in fact, have provided numerous substantial utilities. Accordingly, Applicants have complied with the substantial utility requirement.

The Claimed Invention Has A Credible Utility

In addition to a specific and substantial utility, the Utility Examination Guidelines require that such utility be credible (a "credible utility"). That is, whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. Clearly, the numerous specific and substantial utilities asserted by Applicants are credible.

Assertions of utility are credible unless "(A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based is inconsistent with the logic underlying the assertion." (See, Revised Interim Utility Guidelines Training Materials.) Further, the PTO is reminded that it ***must*** treat as true a statement of fact made by Applicants in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis

to doubt the credibility of such a statement. All the utilities described for the polypeptide are based on sound logic. Furthermore, the utilities for the claimed polypeptides are ***not*** inconsistent with the logic underlying the assertion that the polypeptides are useful. Polypeptides are useful to generate antibodies, identify ligands or protein partners, evaluate expression patterns, evaluate protein activity, etc. The Office has provided no evidence that the logic is seriously flawed or that the facts upon which these assertions are based are inconsistent with the logic underlying the assertions.

Furthermore, GPCR proteins have a well-established utility. Many medically significant biological processes are mediated by signal transduction pathways involving G-proteins and other second messengers, and G protein coupled seven transmembrane receptor proteins are recognized as important therapeutic targets for a wide range of diseases. According to a recently issued United States patent, nearly 350 therapeutic agents targeting GPCRs have been successfully introduced onto the market in only the last fifteen years. (See U.S. Patent No. 6,114,127, at col. 2, lines 45-50.) A recent journal review reported that most GPCR ligands are small and can be mimicked or blocked with synthetic analogues. That, together with the knowledge that numerous GPCRs are targets of important drugs in use today, make identification of GPCRs "a task of prime importance." (See, Marchese et al., Trends Pharmacol. Sci., 20(9): 370-5, 1999, attached hereto). Thus, the allegation that there is no well established utility for proteins of the class that the Applicants are now claiming is directly refuted by industry evidence.

In this respect, the G protein coupled receptor family is analogous to the chemical genus that was the subject of *In re Folkers*, 145 USPQ 390 (CCPA 1965) (Compound that belongs to class of compounds, members of which are recognized as useful, is considered useful under §101.) The Patent Office does not serve the public by attempting to substitute a formulaic analysis of § 101 for the established judgment of the biopharmaceutical industry as to what is "useful." If the Patent Office is aware of any well-grounded scientific literature suggesting that GPCR's are not useful, Applicants request that it be made of record.

Art-Recognized Utility

The Utility requirement may also be satisfied by an "Art Established Utility" which means that "a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention... and the utility is specific, substantial and credible." (M.P.E.P. §2107).

Applicants note for the record that the Patent Office apparently agrees with Applicants' reasoning that GPCRs are useful in that the Office has granted and apparently continues to grant patents to G-protein coupled receptors, their encoding polynucleotides and antibodies directed to them ***in which no natural substrate or specific biological significance*** is ascribed to the GPCR. Specifically, Applicants would like to bring the following US Patents to the Office's attention:

6,518,414 Maclennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims an isolated polynucleotide)
6,511,826 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor (CCR5) HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
6,372,891 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims an antibody directed to a G-protein coupled receptor)
6,361,967 Agarwal et al. "AXOR10, A G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
6,348,574 Godiska et al. "Seven Transmembrane Receptors" (Claims an antibody directed to a G-protein coupled receptor)
6,114,139 Hinuma et al. "G-Protein Coupled Receptor Protein and A DNA Encoding the Receptor" (Claims an isolated polynucleotide).
6,111,076 Fukusumi et al. "Human G-Protein Coupled Receptor (HIBCD07)" (Claims isolated polypeptide)
6,107,475 Godiska et al. "Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)
6,096,868 Halsey et al. "ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims isolated polypeptide)
6,090,575 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPR1" (Claims isolated polynucleotide)
6,071,722 Elshourbagy et al. "Nucleic Acids Encoding A G-Protein Coupled 7TM Receptor (AXOR-1)" (Claims an isolated polynucleotide)
6,071,719 Halsey et al. "DNA Encoding ECR 673: A 7-Transmembrane G-Protein Coupled Receptor" (Claims an isolated polynucleotide)
6,060,272 Li et al. "Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)

6,048,711 Hinuma et al. "Human G-Protein Coupled Receptor Polynucleotides" (Claims isolated polynucleotide)
6,030,804 Soppet et al. "Polynucleotides Encoding G-Protein Parathyroid Hormone Receptor HLTDG74 Polypeptides" (Claims isolated polynucleotide)
6,025,154 Li et al. "Polynucleotides Encoding Human G-Protein Chemokine Receptor HDGNR10" (Claims an isolated polynucleotide encoding a protein identified as a "chemokine receptor" with no specific chemokine identified)
5,998,164 Li et al. "Polynucleotides Encoding Human G-Protein Coupled Receptor GPRZ" (Claims isolated polynucleotide)
5,994,097 Lal et al. "Polynucleotide Encoding Human G-Protein Coupled Receptor" (Claims isolated polynucleotide)
5,958,729 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polypeptide)
5,955,309 Ellis et al. "Polynucleotide Encoding G-Protein Coupled Receptor (H7TBA62)" (Claims isolated polynucleotide)
5,948,890 Soppet et al. "Human G-Protein Receptor HPRAJ70" (Claims isolated polypeptide)
5,945,307 Glucksmann et al. "Isolated Nucleic Acid Molecules Encoding A G-Protein Coupled Receptor Showing Homology to The 5HT Family of Receptors" (Claims isolated polynucleotide)
5,942,414 Li et al. Polynucleotides Encoding Human G-Protein Coupled Receptor HIBEF51" (Claims isolated polynucleotide)
5,912,335 Bergsma et al. "G-Protein Coupled Receptor HUVCT36" (Claims isolated polynucleotide)
5,874,245 Fukusumi et al. "Human G-Protein Coupled Receptors (HIBCD07)" (Claims isolated polynucleotide)
5,871,967 Shabon et al. "Cloning of A Novel G-Protein Coupled 7TM Receptor" (Claims isolated polynucleotide)
5,869,632 Soppet et al. "Human G-Protein Receptor HCEGH45" (Claims isolated polynucleotide)
5,856,443 MacLennan et al. "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,834,587 Chan et al. "G-Protein Coupled Receptor, HLTEX11" (Claims isolated polypeptide)
5,776,729 Soppet et al. "Human G-Protein Receptor HGBER32" (Claims isolated polynucleotide)
5,763,218 Fujii et al. "Nucleic Acid Encoding Novel Human G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,756, 309 Soppet et al. "Nucleic Acid Encoding A Human G-Protein Receptor HPRAJ70 and Method of Producing the Receptor" (Claims isolated polynucleotide)
5,585,476 MacLennan "Molecular Cloning and Expression of G-Protein Coupled Receptors" (Claims isolated polynucleotide)
5,759,804 Godiska et al. "Isolated Nucleic Acid Encoding Seven Transmembrane Receptors" (Claims isolated polynucleotide and methods)

Applicants submit that these issued US Patents are evidence of an art recognized utility for G-protein coupled receptors whose natural ligand is unknown. If the Patent Office's position is that issued patents are ***not*** sufficient evidence of art recognition then Applicants respectfully request that this position be made of record. In the alternative, if the Patent Office wishes to take the position that these issued patents are directed to non-statutory subject matter, then Applicants respectfully request that this position be made of record as well.

In view of the foregoing, Applicants respectfully requests that the rejection under 35 U.S.C. § 101 be withdrawn.

Rejections under 35 U.S.C. § 112

Claims 30-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to adequately teach how to use the instant invention "for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101." (Office Action, page 6). Applicants respectfully disagree.

As discussed above, the present invention ***is*** supported by a specific, substantial, and credible asserted utility as well as a well-established utility. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claims 30-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly subject matter which was not was described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. According to the Office:

> These claims encompass an isolated polypeptide comprising an amino acid sequence "homologous" to the amino acid sequence presented in SEQ ID NO:2 of the instant application...The instant specification, however, only contains an adequate written description of a single protein within the recited genus and this protein comprises the amino acid sequence presented in SEQ ID NO:2. No homologous protein...is adequately described in the instant specification...Because the instant specification does not identify that structural feature or combination of features which define the genus of claimed

> polypeptides...as required by the first paragraph of 35 U.S.C. § 112 it does not provide adequate written support for the breadth of the instant claims.

(Office Action, page 7). Applicants respectfully disagree.

According to the M.P.E.P:

> An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

(M.P.E.P § 2163). The pending claims demonstrate that Applicants were in possession of the claimed invention at the time the application was filed because the claims contain "descriptive means" that define the claimed invention.

For example, claim 30 recites, "An isolated polypeptide comprising SEQ ID NO:2 or a fragment thereof, wherein said polypeptide comprises an epitope specific to SEQ ID NO: 2." The term "epitope specific" is defined on page 23 of the present application and would be readily understood by one of ordinary skill in the art to provide structural and functional characteristics of the invention.

Claims 33 refers to an isolated polypeptide that is at least 80% homologous to SEQ ID NO:2. Claim 80 refers to an isolated polypeptide that is at least 90% homologous to SEQ ID NO:2. Claim 32 refers to a peptide that is at least 95% identical to SEQ ID NO:2. A person of ordinary skill in the art would understand that the "descriptive means" of the pending claims include that the isolated polypeptide is at least 80% homologous to, at least 90% homologous to, or at least 95% identical to SEQ ID NO:2. A person of ordinary skill in the art would understand that further "descriptive means" of the genus are provided in claim 81 (that the protein is a seven transmembrane receptor) and in claim 82 (that the isolated polypeptide is a G-protein coupled receptor). Claim 85 also has "descriptive means" that define the genus of the claimed polypeptides." Claim 85 recites:

> A purified and isolated polypeptide encoded by a polynucleotide comprising a nucleotide sequence wherein said polynucleotide hybridizes to the nucleotide sequence set forth in SEQ ID NO: 1 or the noncoding strand complementary thereto, under stringent hybridization conditions with the provision that the polynucleotide comprises a nucleotide sequence that differs from the sequence

set forth as SEQ ID NO: 1 and from its complementary strand by at least one nucleotide.

The "descriptive means" set forth in claim 85 allow a person of ordinary skill in the art to readily understand that the defining characteristics of the claimed invention. A person of ordinary skill in the art would understand that Applicants had possession of the claimed invention. The "descriptive means" set forth clearly show possession of the claimed invention.

Thus, Applicants have clearly shown that they had possession at the time the application was filed. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

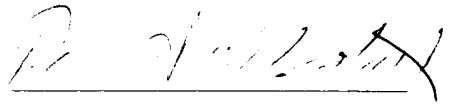
Claims 30-35 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Office, "Claims 30 to 35 are vague and indefinite in so far as they rely upon the term "an amino acid sequence homologous to a sequence of SEQ ID NO:2" and for allegedly employing "the term nGPCR-2644 as a limitation." (Office Action, pages 8-9). Applicants respectfully disagree.

Applicants have amended the claims to further clarify the claim language, rendering the rejection moot. In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. § 112, second paragraph be withdrawn.

Conclusion

Applicants believe the claims are in condition for allowance. An early Notice of Allowance is therefore earnestly solicited. Applicants invite the Examiner to contact the undersigned at (215) 665-6928 to clarify any unresolved issues raised by this response.

Respectfully submitted,



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Attachments: Marchese *et al.*, *Trends Pharmacol. Sci.*, 20(9): 370-5, 1999